

Acute Coronary Vasospasm Resulting from Sumatriptan Administration in a Patient with Raynaud's Disease

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Raynaud's phenomenon is characterized by episodic digital ischemia secondary to marked vasospasm and is usually precipitated by cold exposure or emotional stress. Raynaud's disease is the idiopathic version of Raynaud's phenomenon. Migraine headaches and variant angina occur frequently in patients who have Raynaud's disease. These symptoms suggest a common etiology of increased sensitivity to vasoactivity.^{1,2}

A specific 5-hydroxytryptamine-1 receptor agonist, sumatriptan succinate is used commonly in the treatment of migraine headaches. The main therapeutic pharmacologic action of this drug is effected through arteriolar vasoconstriction.³ Serious adverse cardiac effects have been associated with sumatriptan use in some patients.⁴⁻⁷ This article reports the first case of a patient with Raynaud's disease who had an acute coronary vasospasm secondary to administration of sumatriptan.

CASE PRESENTATION

A previously healthy 44-year-old woman went to a local urgent care clinic for treatment of a migraine headache that had been present for 3 days. She said this headache was typical of previous migraines. She was not using any chronic medications and had taken only acetaminophen and ibuprofen for the headache, without improvement in symptoms. She reported no other significant medical history. Her only reported coronary risk factor was a smoking history of 10 cigarettes per day for the past 5 years. Family history was negative for coronary artery disease. She exercised routinely without any shortness of breath, dizziness, or chest discomfort. Her last menstrual period had occurred 10 days previously and had been normal.

She was treated with sumatriptan 6 mg subcutaneously. Ten minutes postinjection, the patient reported nausea, shortness of breath, and severe central

chest discomfort radiating to both arms. She also became diaphoretic. An electrocardiogram was obtained (**Figure 1**), which showed 4 mm of acute ST elevations in the inferior leads, 3 to 5 mm of ST depression, and T wave inversions in the anterior and lateral leads. She was given aspirin 325 mg orally and nitroglycerin 0.4 mg sublingually; repeat doses were administered 5 minutes later. She was then transferred to the emergency department of a local hospital.

On arrival in the emergency department, the patient disclosed a medical history of Raynaud's disease, established after she had had several episodes of intense digital vasospasm. Physical examination in the emergency department revealed a patient in mild distress reporting continued left arm pain. Oral temperature was 36.7°C (98.1°F), blood pressure was 129/76 mm Hg, pulse was 72 bpm, and respirations were 16 breaths/min. Pulse oximetry measurement while the patient breathed room air was 100%. Results of skin examination were significant for slight diaphoresis. Results of examination of the head, ears, eyes, and throat were unremarkable. The neck was supple, with no jugular venous distension. On auscultation, the lungs were clear; heart examination revealed a regular rhythm with no clicks, snaps, gallops, or murmurs. Results of abdominal and back examinations were benign. Her extremities showed no cyanosis, clubbing, or edema, and peripheral pulses were intact. A rectal examination was heme negative.

Laboratory testing showed that leukocyte count, hemoglobin level, hematocrit, prothrombin time,

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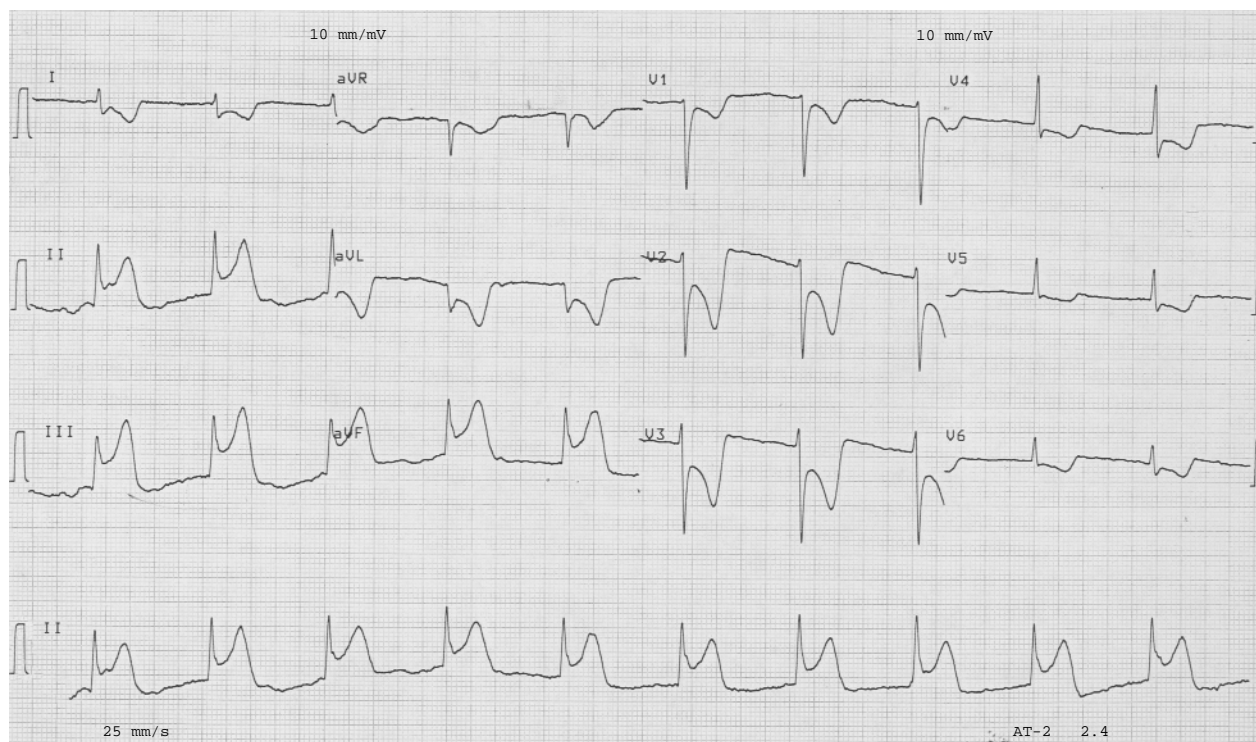


Figure 1. Initial electrocardiogram of the case patient showing acute ST elevations in the inferior leads, ST depressions, and T wave inversions in the anterior and lateral leads.

partial thromboplastin time, and serum electrolyte levels were all within normal limits. Her total lipid profile, including serum cholesterol level, was also within normal limits. Serum creatine kinase level was less than 20 U/L (normal range, 30–135 U/L). A chest radiograph was clear.

The patient was placed on 3 L of nasal oxygen, and intravenous infusion of saline solution and cardiac monitoring were begun. A repeat electrocardiogram was obtained (**Figure 2**), which showed resolving ST segment changes. The patient now stated that her symptoms had completely resolved. She was then given diltiazem 60 mg orally, and a half-inch of nitroglycerin ointment was applied topically.

Cardiology consultation was obtained, and the patient was admitted to the cardiac monitoring unit. Serial measurements of creatine kinase level remained normal over the next 24 hours. Results of a stress echocardiogram were normal, with no signs of ischemia or wall motion abnormalities. The patient refused diagnostic cardiac catheterization. She was provided smoking cessation counseling but declined a medical alert bracelet listing Raynaud's disease as her condition. She has subsequently done well, is still on no medications, and is asymptomatic of any cardiac disease.

DISCUSSION

Description and Epidemiology

Raynaud's disease, the idiopathic variety of Raynaud's phenomenon, is characterized by episodic digital ischemia secondary to marked vasospasm, which is usually precipitated by cold exposure or emotional stress. The phenomenon was first described in 1862 by the French physician Maurice Raynaud after he noted triphasic color changes in the digits of some patients exposed to cold. Raynaud's phenomenon affects 5% of adults, although the great majority of patients are relatively asymptomatic and seek no treatment.⁸ Peripheral vasospasm from Raynaud's phenomenon can be severe enough to cause persistent and complete digital ischemia.

Pathogenesis

The pathogenesis of Raynaud's disease remains unknown, but current research focuses on the following theories: (1) central neurogenic theories, which involve exaggerated reflex sympathetic vasoconstriction and impaired thermoregulation, and (2) "local fault" theories, which note increased sensitivity and levels of α_2 -adrenergic receptors in digital vascular beds of patients with Raynaud's phenomenon. Although the hallmark of Raynaud's phenomenon is digital vasospasm, it is also

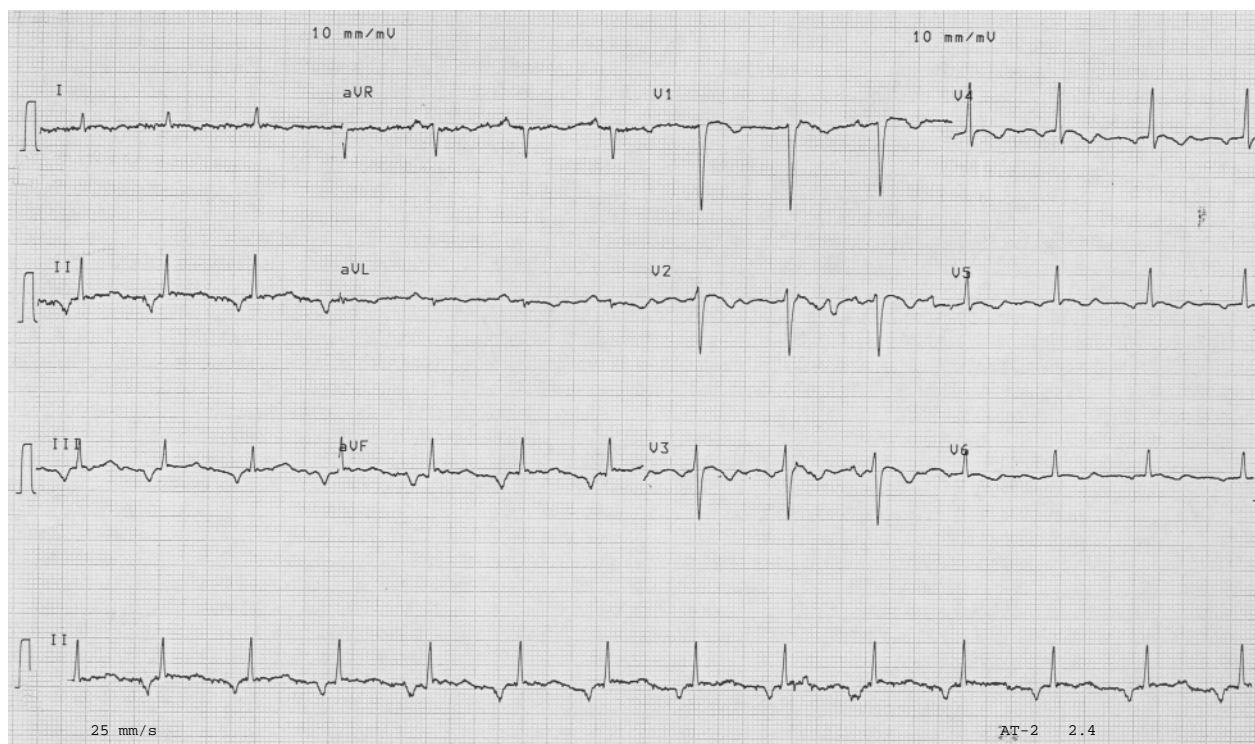


Figure 2. Electrocardiogram of the case patient obtained after administration of nasal oxygen and 2 sublingual doses of nitroglycerin 0.4 mg showing resolving ST segment changes.

known to affect other vascular beds, including the cerebral, cardiac, and pulmonary vasculature.^{2,9} It has been observed that Raynaud's phenomenon occurs more frequently in patients with migraine headaches and variant angina and that Raynaud's symptoms will often resolve after successful treatment for migraines. This observation suggests a common predisposing mechanism for the observed impaired vasoregulation.^{1,10}

Effects of Sumatriptan

Sumatriptan succinate is commonly used in the treatment of migraine headaches. It can be administered orally or subcutaneously; a self-injector for home use is available, as is a nasal spray. When administered subcutaneously, sumatriptan reaches its peak plasma concentration in 12 minutes.³

Sumatriptan's main mode of action is to cause vasoactive contraction of the cerebral vascular beds.³ It is also highly vasoactive in the systemic, coronary, and pulmonary vascular systems when administered subcutaneously or intravenously. MacIntyre and colleagues¹¹ injected 10 patients who had suspected coronary artery disease with sumatriptan 6 mg subcutaneously during coronary angiography. They found that mean coronary artery diameter decreased 16% from baseline at

10 minutes and 17% at 30 minutes postinjection. Although the prescribing information available from the manufacturer advises extreme caution in administration of sumatriptan to patients with any increased risk for or known coronary artery disease, there is no mention of other vasoconstrictive disorders.⁴

A search of the medical literature revealed 4 previous case reports documenting acute coronary spasm or injury secondary to sumatriptan use.^{5,6,12,13} In the first case, a 35-year-old woman with severe occult 4-vessel coronary artery disease had an acute cardiac arrest and myocardial infarction after administration of sumatriptan.⁵ In the second case, a 47-year-old woman with no previous history of ischemic heart disease or variant angina developed an acute transmural myocardial infarction after sumatriptan administration.⁶ In the third case, a 43-year-old man developed a transmural myocardial infarction after taking 100 mg of oral sumatriptan succinate for treatment of a migraine¹²; coronary angiography revealed minor irregularities in his left anterior descending artery. In the fourth case, a 56-year-old woman had a myocardial infarction after treatment with sumatriptan, although results of subsequent cardiac catheterization were within normal limits.¹³ Postmarketing experience cites several other unpublished cases of vasospasm,

dysrhythmia, or myocardial injury following sumatriptan injection, largely occurring in patients later proven to have occult coronary artery disease.⁴

This case is unique because of the patient's Raynaud's disease, which has an increased sensitivity to vasospasm and thus may have substantially predisposed her to coronary artery spasm secondary to sumatriptan administration. Because the patient refused diagnostic cardiac catheterization, occult coronary artery disease could not be ruled out with an absolute degree of certainty. However, given that her only major risk factor for occult coronary artery disease was a minor smoking history, coronary artery disease is unlikely in this patient. Her age, sex, premenopausal state, negative family history, and normal stress echocardiogram place her at low risk for occult coronary artery disease.

CONCLUSION

Sumatriptan has been associated with serious adverse cardiac effects by both direct and temporal relationships. It should be used with caution, especially in any patients with even minor risk factors for occult coronary artery disease. Investigation for the presence of Raynaud's phenomenon/disease or other vasoactive disorders should be a part of the routine history before sumatriptan is administered. We further recommend that sumatriptan be used with extreme caution in patients with Raynaud's phenomenon/disease until further study can quantify the increased risk of coronary vasospasm for these patients. **HP**

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